20.1 Introduction

Binglang, Semen Arecae, is the dry mature seed of Areca catechu L. (Palmaceae) collected between late spring and early fall. It is recommended in traditional Chinese medicine as an anthelminthic, antimalarial, antidysenteric, and digestant for treatment of ascaris, tapeworms, fasciolopsiasis, malaria, dysentery, and dyspepsia.

Dafupi, Pericarpium Arecae, is the dry pericarp of the mature or immature fruits and is mainly used as a diuretic for treatment of edema.

20.2 Chemical Constituents

The areca nut is well known to contain a number of closely related alkaloids with a pyridine ring. The major alkaloid arecoline (20-1) was first reported about 100 years ago [1–3]. Later, arecaidine (20-2) [2–4], guvacine (20-3) [4–6], guvacoline (20-4) [7], arecolidine (20-5) [8], and isoguvacine (20-6) [6, 9] were isolated and structurally determined.

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\begin{align*}
\text{Arecoline (20-1)} & \quad \text{Arecaidine (20-2)} & \quad \text{Guvacine (20-3)} \\
\text{Guvacoline (20-4)} & \quad \text{Arecolidine (20-5)} & \quad \text{Isoguvacine (20-6)}
\end{align*}
\]

The total alkaloid content was 0.15%–0.67%, in which 0.07%–0.50% is arecoline. The other five alkaloids are minor components. In addition to alkaloids, tannins, sitosterol, carbohydrate, saponins, and carotene were detected in areca nut [10].

Arecaidine and its methyl ester arecoline could be synthesized from aliphatic compounds either by cyclization or directly from pyridine derivatives [11–19].
20.3 Pharmacology

Alkaloids, especially the most abundant one arecoline, are mainly responsible for the biological significance of the areca nut.

Arecoline hydrobromide was effective in treating tapeworm in geese [20] and dogs [21]. It exerts its anthelmintic action by causing the muscles of cestodes to relax and by causing the host to purge so that detached worms are removed [22]. Oral administration of 40 mg arecoline hydrobromide per dog daily for 5 days completely controlled tapeworm [23]; however, it had a low efficiency against ascaris in dogs [21]. Synthetic arecoline was recommended as an equivalent substitute for the natural compound [24]. In ducks, arecoline hydrobromide had a lethal dose of 7–8 mg/kg; the therapeutic dose was 0.5–1.0 mg/kg [25]. Arecoline is an acaricidal but not an insecticidal agent [26].

Most investigations on the biological activities of arecoline have focused on its neuropharmacologic properties. The central effects of arecoline were mydriasis, induction of behavioral abnormalities, impairment of conditioned reactions, and pseudoanalgesic properties. In mice, arecoline decreased motility, exploratory activity, and enhancement of motility induced by caffeine and amphetamine. These effects were suppressed by atropine but not by methylatropine [27].

Arecoline was similar to pilocarpin in increasing the acetylcholine and hydroxyindoleacetic acid levels in rat brain; however, the effect caused by arecoline could be blocked by atropine [28].

Administration of arecoline at a dose of 10 mg/kg, i.p. into rats age 10–30 days or more than 300 days caused tremors and an increase in cerebral acetylcholine content which was restricted to the telencephalon. In 5-day-old animals the same dose of arecoline caused neither tremors nor changes in acetylcholine content [29]. The intensity of the tremor was dose related, reached its maximum at 2–5 min after arecoline administration, and disappeared within 30 min. At a dose of 0.05 mg/kg, arecoline selectively increased local cerebral glucose utilization in the hippocampus and medial raphe, whereas higher doses produced more generalized metabolic enhancement. The selective increase in local cerebral glucose utilization by a low dose of arecoline in the hippocampus presumably is due to a specific action of arecoline [30].

Arecoline also stimulated the superior cervical ganglion of cats following intraarterial injection into the ganglion [31]. Since the effects of arecoline on the central nervous system are inhibited by atropine, they are presumably mediated by muscarinic receptors [32, 33]. Arecoline increased cGMP levels of rat corpus striatum slices in vitro with an EC50 value of 22 μM. The cGMP response corresponded directly to muscarinic receptor occupancy [34]. Inhibition of the Na+/K+ ATPase activity in rat brain cerebral cortex, striatum, thalamus, hippocampus, and medulla was time dependent following i.p. administration of arecoline at a dose of 5 mg/kg. The greatest decrease of Na+/K+ ATPase activity was detected in those brain structures rich in cholinergic innervation such as the striatum and hippocampus [35].

The cardiovascular effects of arecoline were studied in anesthetized dogs. After i.v. bolus administration of arecoline at dose of 0.01–100 μg/kg, mean arterial blood pressure was immediately reduced within 1 min after each dose but returned to the baseline value by 5 min after doses of 0.01–10 μg/kg, and by 20 min after a 30 μg/kg dose. Blood pressure was still depressed 20 min after a dose of 100 μg/kg. Cardiac